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# The comparison of Alfentanil and Remifentanil infusion during anesthesia on post-anesthesia recovery

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## ABSTRACT

**Background and Objective:** With consideration the daily increased development of outpatient surgeries and high rate of these surgeries in elderly patients, rapid and safe recovery of patients is necessary. In this clinical trial study, recovery time and nausea and vomiting after the use of two rapid-onset narcotics, Alfentanil and Remifentanil, in elderly patients were evaluated. **Methods:** In this double-blind prospective clinical trial, 40 elderly patients (age above 65 years) candidate to cataract surgery with general anesthesia were studied. The patients were divided randomly into two groups and for first group, 10 µg/kg of Alfentanil was injected and for second group Remifentanil 0.5 µg/kg was injected intravenously during 30 seconds one minute before induction. Both two groups were under general anesthesia with same method and during the anesthesia, first group took infusion of Alfentanil 1 µg/kg/min and second group took Remifentanil 0.1 µg/kg/min. In the end of surgery, the time intervals between end of anesthesia drug administration and spontaneous respiration, eyes opening with stimulation, verbal response and discharge of recovery room, also the incidence of complications related to narcotic drugs, especially nausea and vomiting, was recorded. The data were analyzed in SPSS software using descriptive and analytical statistics such as T-test and chi square test. **Results:** The time of spontaneous respiration in Alfentanil group was 2 minutes and in Remifentanil group was 3.3 minutes, the difference was not statistically significant ( $P=0.08$ ). The time of eyes opening with stimulation, verbal response, and discharge of recovery room were not significantly different. During recovery, incidence of nausea and vomiting in Remifentanil group (30% of patients) was significantly more than Alfentanil group (5% of patients) ( $P=0.045$ ). **Conclusions:** Recovery time between Alfentanil and Remifentanil group was not significantly different, but incidence of nausea and vomiting in Remifentanil group was higher than Alfentanil group significantly. It seems that using Alfentanil in the anesthesia for surgical treatment of the elderly people can be preferred.

**Key words:** *Alfentanil, elderly patient, general anesthesia, nausea and vomiting, recovery, Remifentanil*

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## INTRODUCTION

Following laryngoscopy and tracheal intubation, hemodynamic changes in the form of hypertension and tachycardia, cardiac dysrhythmia, catecholamine release,

and myocardial ischemia may be seen. These complications cause health-threatening consequences, especially in the patients with cardiovascular disease.<sup>[1]</sup> Elder person consist higher proportion of people requiring the surgery. These patients usually have lower physiological reserve, variability in autonomic performance, a high prevalence of coexisting cardiovascular diseases, and high sensitivity to the narcotic and anesthetic drugs.<sup>[2]</sup> The narcotics,<sup>[3]</sup> vasodilators,<sup>[4]</sup> beta blockers,<sup>[5]</sup> calcium channel blockers,<sup>[6]</sup> volatile anesthetics,<sup>[7]</sup> local anesthetics,<sup>[8]</sup> alpha blockers,<sup>[9]</sup> and benzodiazepines<sup>[10]</sup> can be used for prevention of these changes.

The administration of pre-anesthetic narcotics is usually used for tolerating the laryngoscopy and tracheal

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intubation. Among these, the Alfentanil and Remifentanil have been more increasingly used recently because of their rapid onset effects than any other narcotics.<sup>[11]</sup>

Narcotics can increase post-anesthetic nausea and vomiting (PONV) with multiple mechanisms including direct effects on receptors in the vomiting center of the brain stem, vestibular sensitive to vomiting caused by motion, increased gastric secretion, decreased gastric motion and emptying of the stomach.<sup>[12]</sup> Given the sensitivity to narcotics in the elderly, increasing outpatient surgeries and patients need rapid return to normal condition after surgery; in recent years, more attention to recovery time and incidence of complications in the elderly has been paid.<sup>[13]</sup> The objective of this study was to compare two narcotics of Alfentanil and Remifentanil in terms of returning time to consciousness following the elimination of anesthesia drugs and PONV incidence in the elderly patients.

## METHODS

After the approval of Local Ethical Committee (in 2009) and obtaining written consent from patients to be studied, 40 patients with physical condition of ASA I-III who were volunteers to cataract surgery in Ardabil's Alavi hospital (in Iran) were studied in a double blind prospective clinical trial. Subjects were randomized to A (Alfentanil) and R (Remifentanil) groups by computer-generated codes in closed envelopes opened just before surgery [Figure 1]. The inclusion criteria for this study were ASA physical class I-III, aged 65-85 years. The exclusion criteria were ASA physical class higher than III, history of respiratory diseases, history of motion sickness, history of PONV, narcotic abuse, hiatal hernia, gastro-esophageal reflux, overweight (BMI>30), being at risk of aspiration, and those having a history of major problem in the previous anesthesia. These trial preparations were prepared by anesthesia nurse who was not involved in the study and who recorded the group randomization separately, such that the anesthesiologist recording the data and caring for the patient was unaware of what the preparation contained. All patients had received ringer 5 ml/kg and 100% oxygen within 3 minutes before induction of anesthesia. The first group (A) received Alfentanil 10 µg/kg and the second group (R) received Remifentanil 0.5 µg/kg within 30 seconds. Both drugs were prepared in the syringe with an equal volume and anesthesiologist injector was not aware of the type of medication. Immediately after receiving the primary total dose of narcotics, 0.5 mg/kg Propofol was injected to the patients of both groups, and then continued with 10 mg/s until the decreasing of verbal response. Then, 1 mg/kg Succinylcholine was injected. The patients were ventilated with 0.6 MAC (Minimum Alveolar Concentration) Halothane and 50% O<sub>2</sub> and 50% N<sub>2</sub>O. To

keep the muscle relax, 0.2-0.3 mg/kg Atracurium was injected. During anesthesia, subjects were infused by Alfentanil 1 µg/kg/min and 0.1 µg/kg/min Remifentanil in groups (A) and (R), respectively. Also, both narcotics were prepared in the syringe with an equal volume. The patients received these two drugs in a randomized manner, which had been prepared and blinded with a blinded hospital pharmacy. The patients were monitored using pulse oximetry, heart rate, blood pressure, and electrocardiographic monitoring during anesthesia. At the end of surgery, all of the anesthetic drugs were discontinued and 100% oxygen with 6 l/min was given to them. Following spontaneous respiration of the patients, the neuromuscular block was reversed by 0.025 mg/kg Atropine and 0.05 mg/kg Neostigmine and patients were extubated after proper position. The period between stopping drugs and returning to the spontaneous respiration was recorded as the respiratory returning time. Then, patients were transferred to recovery room and the intervals were recorded as the time needed between stopping drugs until opening eyes with stimulation and return of verbal response. Finally, the time of stopping of drugs until discharge from recovery room also was recorded. The condition of patients during recovery time was recorded including nausea, vomiting, and respiratory problems. Intense postoperative nausea or existing vomiting was treated with 10 mg Metoclopramide. A power analysis assuming a two-segment difference with a power of 0.9 and  $\alpha < 0.05$  indicated a sample size of 20 patients for each group. The data obtained from groups were compared using SPSS and analyzed with T-test and chi square test [Figure 1].

## RESULTS

This study had recruited 40 eligible patients into two groups: A (Alfentanil) and R (Remifentanil). They underwent the same surgical treatment and there was no significant difference between two groups regarding age, gender, smoking, systolic, diastolic, and mean arterial blood pressure, heart rates of patients before anesthesia, and duration of anesthesia [Table 1].

The average returning time of respiration after discontinuing of the drugs was noticeably shorter in Alfentanil group (2 minutes) than Remifentanil group (3.3 minutes), but it was not statistically significant ( $P=0.08$ ). There was no significant difference in stopping the anesthesia drugs up to opening eyes, return to verbal response, and discharge from the recovery between two groups.

There was no respiratory problems with narcotics in recovery time, but the nausea and vomiting which were noticed in both groups were higher in Remifentanil ( $n=6$ ) compared to Alfentanil ( $n=1$ ) groups ( $P<0.05$ ) [Table 2].

## DISCUSSION

In this study, we investigated the recovery changes between two groups of elderly patients who had received the narcotics of Alfentanil and Remifentanil. We found that the returning time to spontaneous respiration in Alfentanil group was 1.3 minutes shorter than Remifentanil group, 2 minutes compared to 3.3 minutes, respectively, but

this difference was not statistically significant. Moreover, the eyes opening time with stimulus, returning of verbal response, and discharging from recovery had no significant difference between two groups. As regards that both drugs are rapid-onset narcotic, no major differences in the recovery of patients in both groups seems logical. Also, in this study, nausea and vomiting in the Remifentanil group was significantly higher than the Alfentanil group.

These findings are similar to results obtained from several studies. Wiel *et al.* in comparison of a bolus of 30 µg/kg of Alfentanil with 2 µg/kg of Remifentanil in direct laryngoscopy without intubation,<sup>[11]</sup> Schuttler *et al.* in comparison of Remifentanil (1.0 µg/kg) and a continuous infusion of 0.5 µg/kg/min, with a loading dose of Alfentanil (25 µg/kg) and a continuous infusion of 1.0 µg/kg/min in major abdominal surgery,<sup>[14]</sup> Agnew *et al.* in comparison of a bolus of 10 µg/kg of Alfentanil with 1 µg/kg of Remifentanil in outpatient bronchoscopy,<sup>[15]</sup> Wuesten *et al.* in comparison of Remifentanil (loading dose 1 µg/kg; maintenance infusion, 0.25 µg/kg/min) with Alfentanil (loading dose, 50 µg/kg; maintenance infusion, 1 µg/kg/min) in ENT surgery,<sup>[16]</sup> and Chinachoti *et al.* in comparison of Remifentanil 1 mg/kg for bolus injection and a continuous infusion of 0.25-0.5 µg/kg/min, with Alfentanil 20 µg/kg for bolus injection and a continuous infusion of 0.5-1 µg/kg/min in gynecologic laparoscopy<sup>[17]</sup> did not observe any significant differences in cases of recovery between the two drugs.

In Nilsson *et al.*'s study<sup>[18]</sup> in which 58 patients were randomized to receive Propofol and either Remifentanil or Alfentanil as part of a total intravenous anesthesia reported that the interval between stopping the anesthetic drug and extubation of tracheal tube was 5 minutes longer in Remifentanil

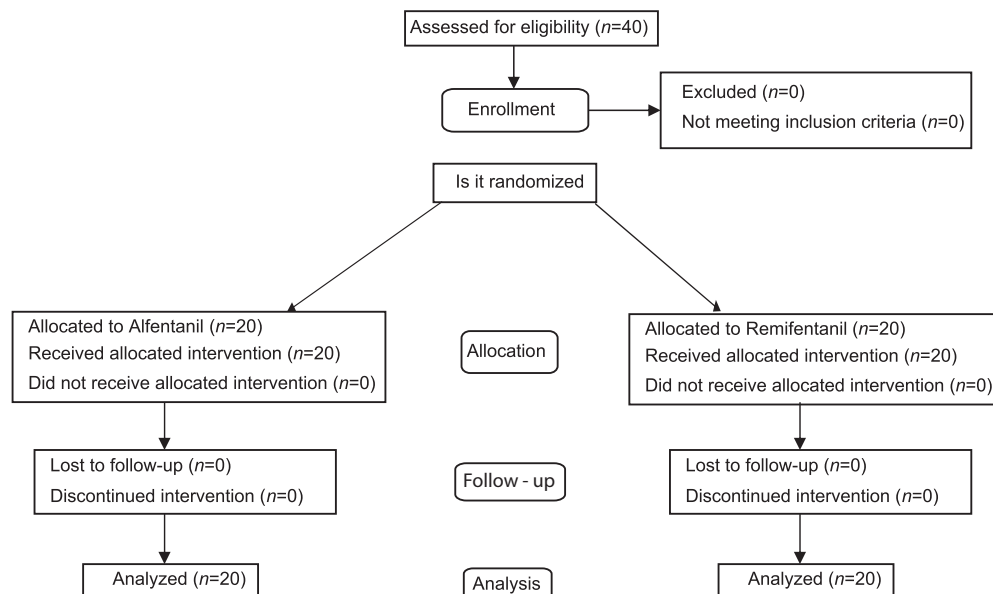
**Table 1: Basic characteristics of patients**

Variable	Group A	Group R	P value
Age (year)	70±5.3	73±6.4	0.37
Gender (female/male)	8/12	9/11	0.26
Smoking (%)	6 (33.3%)	8 (25%)	0.09
Systolic blood pressure (mmhg)	146.5±27.5	137.7±30.1	0.34
Diastolic blood pressure (mmhg)	85.7±14.8	77.5±19.7	0.14
Mean arterial pressure (mmhg)	105.9±18.5	97.5±22.8	0.20
Heart rate (b/min)	68.4±14.7	70.8±13.6	0.59
Anesthesia duration (min)	36.4±5.2	37.8±4.3	0.43

(Mean±SD)

**Table 2: The time average from stopping the anesthetic drugs to return of respiration, eye opening, verbal response and discharge from recovery, and incidence of nausea and vomiting**

Variable	Group A	Group R	P value
Time of respiration return (min)	2	3.3	0.08
Time of eye opening with stimulation (min)	10	7.8	0.18
Time of verbal response (min)	11.4	10.1	0.42
Time of recovery discharge (min)	13.4	12.1	0.40
Nausea and vomiting in recovery (%)	5	30	0.045



**Figure 1: Methodology flowchart**

group, which is similar to our study. In that study, the time interval between stopping the anesthetic drug and discharge from recovery room was similar between the two groups that confirm our study. The relatively long time to return spontaneous breathing after the infusion of Remifentanil in this study can be due to high-dose infusion of this drug.

Also, in this study, nausea and vomiting in the Remifentanil group was significantly higher than the Alfentanil group. It may also be associated with the infusion dose of this drug and may require Remifentanil dose adjustment in subsequent studies. In a study by Gazynski *et al.*,<sup>[19]</sup> the nausea and vomiting rate in Remifentanil group were higher which confirms our study, but these rates were similar in another study by Chinachoti *et al.*<sup>[17]</sup> that probably this difference is due to studying on gynecological surgery and due to the effect of age and sex of patients on postoperative nausea and vomiting.

A limitation of our study may be that we did not follow up patients after recovery for assessing of long-term side effects of these drugs.

## CONCLUSION

Recovery time between Alfentanil and Remifentanil group was not significantly different, but incidence of nausea and vomiting in Remifentanil group was higher than Alfentanil group significantly. It seems that using Alfentanil in the anesthesia for surgical treatment of the elderly people can be preferred. Also, according to high incidence of PONV after using of Remifentanil, we recommend PONV prophylaxis use before using this drug.

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